

1 GAATTCCAGGCTGCTAGGAAGTGAAGTGAACCTGGACCCAGCTCAGCGGCAGCAGCAG 60

61 CCGCAGCAGGCAGCAGCCTCTATCCTCTCCTCCAGCCACATGGGCCCGGATGGCGCTT 120
MetGlyProArgMetAlaLeu

121 CCCCCGCTGCTCCTGCTCCTGTTCTTGCACCTGTTGCTAGGATGCCGTTCCCATCCA 180
ProArgValLeuLeuLeuPheLeuHisLeuLeuLeuGlyCysArgSerHisPro
eProAlaCysSerCysSerCysThrCysCysCysEndAspAlaValProIleHi
erProArgAlaProAlaProValLeuAlaProValAlaAlaArgMetProPheProSert

181 CTGGGTGGCGCTGGCCCTGCAGAACTGCCAGGGATACAGGTGAGCCCTGATGAAC TG 240
LeuGlyGlyAlaGlyLeuAlaSerGluLeuProGlyIleGlnValSerProAspGluLeu
sTrpValAlaLeuAlaTrpProGlnAsnCysGlnGlyTyrArgEndAlaLeuMetAsnC
hrGlyTrpArgTrpProGlyLeuArgThrAlaArgAspThrGlyGluProEndEndThra

241 CTTAGACTTGGTGGGAGGGCGGACAGCAGCAACTAACGGGTCCCCACCTACTG 300
LeuArgLeuGlyTrpLeuGlyGlyArgGlyGlnGlnGlnLeuThrGlyProHisLeuLeu
sLeuAspLeuValGlyTrpGluGlyAlaAspSerSerAsnEndArgValProThrTyrCy
laEndThrTrpLeuAlaGlyArgAlaArgThrAlaAlaThrAsnGlySerProProThrV

FIG.1A

301 TTCCAAGAGGGCTCTAACCTCCTTTGGGAACTAGTGATAAGGGGTTTAGAAGGCAGCCAG 360
 PheGlnGluGlySerAsnLeuLeuTrpGluLeuValIleArgGlyLeuGluGlySerGln
 sSerLysArgAlaLeuThrSerPheGlyAsnEndEndGlyValEndLysAlaAlaAr
 alProArgGlyLeuEndProProLeuGlyThrSerAspLysGlyPheArgArgGlnProG

361 GCTGGGGGTGAGGACCCGCTCCCAAGGCAGTTGGTTGGCTTCAGCACCATCAAGAGTGAT 420
 AlaGlyGlyGluAspProLeuProArgGlnLeuValArgPheSerThrIleLysSerAsp
 gLeuGlyValArgThrArgSerGlnGlySerTrpPheAlaSerAlaProSerArgValMe
 lyTrpGlyEndGlyProAlaProLysAlaValGlySerLeuGlnHisGlnGluEndT

421 GGTCCAGGTCCGAGTTCCTGAGGCTCGGGCTCCCCACCCATCCCAGGAGCTGCTGGAC 480
 GlySerArgCysGluPheLeuArgLeuGlyLeuProHisProSerGlnGluLeuAsp
 tGlyProGlyAlaSerSerEndGlySerGlySerProThrHisProArgSerCysTrpTh
 rpValGlnValArgValProGluAlaArgAlaProProIleProGlyAlaAlaGlyP

481 CGCCTGCGAGACAGGGTCTCCGAGCTGCAGGCGGACGGGACCTGGAGCCCCCTCCGGC 540
 ArgLeuArgAspArgValSerGluLeuGlnAlaThrGlyArgThrTrpSerProSerGly
 rAlaCysGluThrGlySerProSerCysArgArgAspGlyProGlyAlaProProAl
 roProAlaArgGlnGlyLeuArgAlaAlaGlyAspGlyThrAspLeuGluProLeuArgG

541 AGGACCTGGCCTCACAGAAGCCTGGGAGCGGAGGAGGAGCCCCACGGGGTCTTTC 600
 ArgThrValAlaSerGlnLysProGlyArgArgGlyLysGlnProProArgGlyPheLeu
 aGlyProTrpProHisArgSerLeuGlyGlyGluGlySerSerProHisGlyGlySerTr
 lAspArgGlyLeuThrGluAlaTrpGluAlaArgGluAlaAlaProThrGlyValLeuG

FIG.1B

601 GGGCCCGCAGTAGCATCTTCCAAGTCTCCGGGGAATACGCAGCCCCAAGACGATGCGTG 660
 GlyProAlaValAlaSerSerLysSerSer
 pAlaProGlnEndHisLeuProSerProPro
 lyProArgSerSerIlePheGlnValLeuArgGlyIleArgSerProLysThrMetArgA

661 ACTCTGGCTGCTTTGGGCGGAGGCTGGACCGGATCGGCTCCCTCAGCGGCTGGGCTGCA 720
spSerGlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyLeuGlyCysA

721 ATGGTGAGCACCCACCCCATTTCCCACTGCACGCCCGGTTAGCATCACTTCTGGGTTTGA 780
snV

781 TGTCTCTGGGACCAAACTCCGAGAAAGGACACCTGGATATCACTCTTCTTGTGCCAG 840

841 TCCTCAAGGCCCAAGGAGCGCCTTCCCTGGAAAAATTAAATTTGGACAGCAATCACTAGCAT 900

901 GACTATGAGTCCCCACCCACCTTCTCGCCACCCCTGCCCTCTCTCACCCCAAGCGGCAGA 960

961 ATTACTTTAGGATGTAAATTCTGTGTCATTGCCCTGGCTGCCGCTCCTGGGAGCAAAAAGAGA 1020

FIG.1C

Genetic

1021 ACTAAACCTCTTCCCCTGGTTTCCCCTCAACTGTCTGTGGCTGCAAGGCAGAGGCAG 1080
 1081 GATCACCAGGTGATGACAAGTCCCAGCTTACAAGGAGGAACTCAGGTCCAGAGAGATG 1140
 1141 GATTATCCCAAGCCCCAACATCCAGTTCTGCTGAAGAAGCGGGTGGCAGGGGTGGCA 1200
 1201 CGTGGTGGGGGAAGCCAGGTCCTGCTGCCTCTCACCCCTAATGTCATCCTCACCCCTCT 1260
 1261 CTCTCCCCCCACAGTGCTCAGGAGGTACTGAGAAGTCCCTGGCTGACAACTCTGTGTCC 1320
 alLeuArgArgTyr**
 1321 GCTTCTCCAAGCCCCCTCCCCTGCTCCCCCTTCAAAGCAACTCCTGTTTTTATTATGTAT 1380
 1381 TTATTTTATTTATTATTGTTGGTTGTATATAAGACGGTCTTATTGTGAGCACATTTT 1440
 1441 TTCCATGGTGAAATAAGTCAACATTAGAGCTCTGTCTTTTGAAAAAATAAAAAAAGGA 1500

1501 ATTC 1504

FIG.1D

BNP Screening Oligos

5'-TCCAGCTGCTTCGGGGCAGGATGGACAGGATTGGAGCCAGAGCGGACTGGGCTGTAAAC-3' human ANP
 SerSerCysPheGlyGlyArgMetAspArgIleGlyAlaGlnSerGlyLeuGlyCysAsn-3' human ANP
 (21)
 SerGlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyLeuGlyCysAsn pig BNP
 5'-ACNGGNTGCTTGGGNCGNCNCTNGACCGNATNGGNTCNCNTTCNGGNCCTNGGNTGCCAAC-3' Pig BNP
 TG T A A A T TA AG T AG T T T
 3'-AGGCCGACGAAGCCCGCTCCGACCTGTCCTAACCTAGGACTCGCCCTGACCCGACATTG-5' 3351 (minimal)
 3'-TCGCCGACGAAGCCGTCTTCTGAGCTGTCTTAGCCGTGGAGTCGCCGGAGCCGACGTTG-5' 3352 (G/T pref)
 3'-AGGTCGACGAAGCCCCCGTCTACCTGTCTCTAACCTCGGGTCTCGCCCTGACCCGACATTG-5' 3376 (ANP)

FIG.2

FIG. 3A

FIG. 3A

50. 60. 70.
 631 CGGGGAATACGCAGCCCAAGACGATGCGTGAAGCTCTGGCTGCTTTGGGGGAGGCTGGACCGGATCGGCT 700
 ArgGlyIleArgSerProLysThrMetArgAspSerGlyCysPheGlyArgArgLeuAspArgIleGlyS
 701 CCCTCAGCGGCTGGGCTGCAATGGTGAGCACCCACCCCAATTCCTCCACTGCACGCCCGGTTAGCATCAC 770
 erLeuSerGlyLeuGlyCysAsnV
 771 TTCTGGGTTTGATGTCTCTGGGGACCAAACTCCGAGAAAAGGACACCTGGATATCACTCTTTCTTGTGTC 840
 841 CAGTCCTCAAGGCCAAGGAGCGCCTTCCTGGAAAAATTAAATTTGGACAGCATTCACTAGCATGACTATG 910
 911 AGTCCCCACCCACCTTCTCGCCACCCCTGCCTCTCTCACCCCAAGGGCGGAGAAATTACTTTAGGATGTAA 980
 981 ATTCTGTCAATTGCTGCGCTCCTGGGAGCAAAAGAGAACTAAACCTCTTCCCCCTGGTTTCCCC 1050
 1051 TCAACTGTCTGTGGCTGCAAGGCAGAGGGCAGGATCACCCAGGGTGATGACAAGTCCCAGCTTACAAGGA 1120
 1121 GGAAACTCAGGTCCAGAGAGATGGATTATCCCAAGCCCCCAACATCCAGTTCTGTGTAAGAAGCGGGT 1190
 1191 GGCAGGGGTGGCAGTGTGGGGGAAGCCAGGTCCTGCCTGCCTCTCACCCCTAATGTCATCCTCACCC 1260
 1261 TCTCTCTCCCCCACAGTGTCTCAGGAGGTACTGAGAAGTCTCTGGCTGACAACCTCTGTGTCCGCTTCTC 1330
 alleuArgArgTyr***
 1331 CAACGCCCTCTCCCTTCAAAGCAACTCCTGTTTTTATTTATTTATTTATTTATTTATT 1400
 1401 TGGTGTGTATATAAGACGGTTCTTATTGTGAGCACATTTTTCCTGATGGTGAATAAAGTCAACATTA 1470
 1471 GAGCTCTGTCTTTTGAAAAAAGGAATTC 1507

FIG.3B

Mature Pig BNP cDNA (10-13-88)

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1  GAATTCAGGCTGCTAGGAAGTGAAAAGTGAACCTGGACCCAGCTCAGCGGCAGCAGCAGCGGCAGCAGG  70
71  CAGCAGCCTCTATCCTCTCCTCCAGCCACATGGGCCCCCGGATGGGGCTTCCCCGGCTGCTCCTCCTCCT  140
    MetGlyProArgMetAlaLeuProArgValLeuLeuLeuLeuLeu
141  GTTCTTGACCTGTTGCTAGGATGCCGTTCCCATCCACTGGTGGCGCTGGCCTGGCCTCAGAACTG  210
    uPheLeuHisLeuLeuLeuLeuGlyCysArgSerHisProLeuGlyGlyAlaGlyLeuAlaSerGluLeu
    ↓1
211  CCAGGGATACAGGAGCTGCTGGACCGCCTCGGAGACAGGGTCTCCGAGCTGCAGGGCGGACGGGACC  280
    ProGlyIleGlnGluLeuLeuAspArgLeuArgAspArgValSerGluLeuGlnAlaGluArgThrAspL
281  TGGAGCCCTCCGGCAGGACCGTGGCTTCACAGAAAGCTGGGAGCGGAGGAGAGCAGCCCCACGGGGT  350
    euGluProLeuArgGlnAspArgGlyLeuThrGluAlaTyrGluAlaArgGluAlaAlaProThrGlyVa
351  TCTTGGGCCCCGAGTAGCATCTTCCAAAGTCTCCGGGAATACGCAGCCCCAAGACGATGCGTGACTCT  420
    lLeuGlyProArgSerSerIlePheGlnValLeuArgGlyIleArgSerProLysThrMetArgAspSer
    ↓2
421  GGCTGCTTTGGCGGAGGCTGGACCGGATCGGCTCCCTCAGCGGCCCTGGGCTGCAATGTGCTCAGGAGGT  490
    GlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyLeuGlyCysAsnValLeuArgArgT
491  ACTGAGAAAGTCTGGCTGACAAACCTCTGTGTCGGCTTCTCCAACGCCCTCCCTGCTCCCTTCAAAGC  560
    yL***
561  AACTCCTGTTTTTATTATGATTTATTATTATTATTATTATTGTTGTATATAAGACGGTCTTATT  630
631  GTGAGCACATTTTTTCCATGGTGAAATAAAGTCAACATTAGAGCTCTGTCTTTTGAAAAAATAAAAAA  700
701  GGAATTC  707

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FIG.4

Dog BNP Gene 12-12-88

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1  CGATCAGGGATGTTGGGCGGAGGAAACGGAGGGAAGGAGCGGAGGAGCCCGAGGACTGTTGGTG 70
71  TCCCCCTCCTGCCCTTTTGGGGCCAGGCCCACTTCTATACAAGCCCTGCTCTCCAGCCTCCACCCCGCG 140
141  GGTATGGTGCAGGCGGAGGGGCGCATTTCCCCCGCCCTGAGCTCAGCGGCCGGAATGGGCCGATAAAT 210
211  CAGAGATAACCCCGAGGCGGGGATAAGGGATAAAAGCCCCCGTTGCCGCGGGATCCAGGAGAGCACCCG 280
281  CGCCCCAAGCGGTGACACTCGACCCCGGTGCGAGCGCAGCAGCTCAGCAGCCCGGACGTCTCTTTCCCCC 350
351  TTCTCTCCAGGACATGGAGCCCTGGCAGCGCTGCCCGGGCCCTCCTGCTCCTCTGTTCTTGCACCT 420
      MetGluProCysAlaLeuProArgAlaLeuLeuLeuPheLeuHisLe
421  GTCGCCACTCGGAGGCGCGCCACCCGCTGGGGCGCGCAGCCCCCGCTCGGAAGCCTCGGAAGCCTCA 490
      uSerProLeuGlyGlyArgProHisProLeuGlyGlyArgSerProAlaSerGluAlaSerGluAlaSer
491  GAAGCCTCGGGGTTGTGGGCGGTGCGAGGTGAGCGCTCAGCCTGCCCTGAAGCCCGCGGGTGGCAGCAG 560
561  GTCACGGGGGCTTAGCCACTGTCCCAAGTCTCCTCAGTCTCCTCTGGGAATTAGTGATAAGGGAATCAGAAA 630
631  GTGACGAGATTGGGTGCCAGGACTCCATACCCAAGGGCGGCTTCACTTGGGTGCAAGGTGTTCCGC 700
701  CCCGGCGTGGTTCTGAGGCTCAGGCGGTCCATTGCAGGAGCTGCTGGGCCGTCTGAAGGACGAGTTT 770
      GluLeuLeuGlyArgLeuLysAspAlaValS

```

FIG.5A

euGlyCysAsn

771	CAGAGCTGCAGGCAGAGCAGTTGGCCCTGGAACCCCTGCACCGGAGCCACAGCCCCGAGAGCCCCCGGA	840
	erGluLeuGlnAlaGluGlnLeuAlaLeuGluProLeuHisArgSerHisSerProAlaGluAlaProGl	
841	GGCCCGAGGAACGCCCTGGGCTCCTTGACCCCATGACAGTGTCTCCAGGCCCTGAGAAGACTACGC	910
	uAlaGlyGlyThrProArgGlyValLeuAlaProHisAspSerValLeuGlnAlaLeuArgArgLeuArg	
911	AGCCCCAAGATGATGCACAAGTCAGGGTGCTTTGGCCGGAGGCTGGACCGGATCGGCTCCCTCAGTGGCC	980
	SerProLysMetMetHisLysSerGlyCysPheGlyArgArgLeuAspArgIleGlySerLeuSerGlyL	
981	TGGGCTGCAATGGTAAGCCGCCCTCCCTGCGGCCTTGGCTCCCCCTCCCGAGCCCCCTGGGTTGACACCTT	1050
	euGlyCysAsnV	
1051	GGAACCCCTTCTGGGTTTGTGTCTCGGGGGATCACACTCTGAGGAAAGGACATCTGGACATCGCTCCTT	1120
1121	CTTGCTGACAGTCCTAAGGGCCCAAGGAGTAGCTTTCTGGAAATACTACGTGTGGACATCGTTGTCCAGGG	1190
1191	TCCCTACCCACCTCCTAGCCCCCTCCTGCCTCTCGCACCCCAAGGGCAGAAATCATCTTAGGATGGAATCA	1260
1261	GTCGTTGTCTGGAAGCATCTCCTTGGAGCAGAAAGAGTCCTAAACATCGTCTCCTAGCTCTCTCTGTCT	1330
1331	GTCTGTAGCCACGAAGGCAGAGGTCAGGGTCAACAGGGCAGTGATGATCCAGTTAACAGAGGAGGAGA	1400
1401	CTGAGGCTCTAGAGAGATGGATTATTCCAAAGCCCTCAACATCCAGATCGGCTGAGGGTGGGTTGGTGGC	1470
1471	AGGGATGGCTCCTGGGCTTGGGAAGCTCGGATCCTGCCTCAGTCTCCACCTGACGCCCATCATCCCCCTC	1540
1541	TCTCTCCTCCCACAGTGTGAGAAAGTATTAAAGGAGGAAGTCCCGACTGCCACATCTGCATTGGATTCT	1610

FIG.5B

alLeuArgLysTyr***

1611	TCAGCAGCCCCCTGAGCCCCCTTGGAAGCAGATCTTATTATTCGTATTATTATTATTATTATTTCGATTG	1680
1681	TTTTATATAAGATGATCCTGACGCCCGAGCACGGATTTCCACGGTGAAATAAAGTCAACCTTAGAGCTT	1750
1751	CTTTTGAAACCGATTGTGTCCTGTGCATTAAAGTAACACATCATTTAAAAAAA	1804

FIG.5C

Human						Dog Hind
Bam	Pst	Eco	Pvu	Stu	Bgl	

Human						Dog Hind
Bam	Pst	Eco	Pvu	Stu	Bgl	

FIG.6

Human BNP Gene 12-12-88

```

1  CCCACGGTGTCCCGAGGAGCCAGGAGGACACCCCGCAGGCTGAGGGCAGGTGGAAGCAAACCCGGACG  70
71  CATCGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCCTCCGCAGTCCCTCCAGAGACATGGATC  140
    MetAspP
141  CCCAGACAGCACCTTCCCGGGCGCTCCTGCTCCTGCTCTTCTTGTCATCTGGCTTTCCTGGAGGTGTTTC  210
    roGlnThrAlaProSerArgAlaLeuLeuLeuPheLeuHisLeuAlaPheLeuGlyGlyArgSe
211  CCACCCGCTGGGCAGCCCCGGTTACGCCCTCGGACTTGGAAACGTCGGGTTACAGGTGAGAGCGGAGGGC  280
    rHisProLeuGlySerProGlySerAlaSerAspLeuGluThrSerGlyLeuGln
281  AGCTCAGGGGATTGGACAGCAGCAATGAAGGGTCTCACCTGCTGTCCCAAGAGGCCCTCATCTTTCC  350
351  TTTGGAATTAGTGATAAAGGAATCAGAAATGGAGAGACTGGGTGCCCTGACCCTGTACCCAAGGCAGTC  420
421  GGTTCACTTGGTGCCCATGAAGGGCTGGTGAGCCAGGGTGGGTCCCTGAGGCTTGGACGCCCCCATTC  490
491  TTGCAGGAGCAGCGCAACCATTTGCAGGGCAAACTGTCCGAGCTGCAGGTGGAGCAGACATCCCTGGAGC  560
    GluGlnArgAsnHisLeuGlnGlyLysLeuSerGluLeuGlnValGluGlnThrSerLeuGluP
561  CCTTCCAGGAGAGCCCCCGTCCACAGGTGTCTGGAAGTCCCGGAGTAGCCACCGAGGGCATCCGTGG  630
    roLeuGlnGluSerProArgProThrGlyValTrpLysSerArgGluValAlaThrGluGlyIleArgGl
631  GCACCGCAAATGCTCCTACACCCCTGCGGGCACCACGAAGCCCCAAGATGTTGCAAGGTCTGGCTGC  700
    yHisArgLysMetValLeuTyrThrLeuArgAlaProArgSerProLysMetValGlnGlySerGlyCys

```

FIG.7A

Sequence

701	TTTGGGAGGAAGATGGACCGGATCAGCTCCTCCAGTGGCTGGCTGCAAAGTAAGCACCCCTGCCAC	770
	PheGlyArgLysMetAspArgIleSerSerSerGlyLeuGlyCysLysV	
771	CCCGGCGCCTTCCCCCATTCAGTGTGTGACACTGTTAGAGTCACCTTTGGGGTTTGTGTCTCTGGGAA	840
841	CCACACTCTTTGAGAAAAGGTCACCTGGACATCGCTTCCTCTTGTTAACAGCCTTCAGGGCCAAGGGTG	910
911	CCTTTGTGGAATTAGTAAATGTGGGCTTATTTCAATTACCATGCCCCACAATACCTTCTCCCCACCTCCTAC	980
981	TTCTTATCAAAGGGGCAGAATCTCCTTTGGGGTCTGTTTATCATTTGGCAGCCCCCAGTGGTGCAGAA	1050
1051	AGAGAACCAACATTTCTCCTCGTTTCTCTAAACTGTCTATAGTCTCAAAGGCAGAGCAGGATCAC	1120
1121	CAGAGCAATGATAATCCCCAATTTACAGATGAGGAACTGAGGCTCAGAGAGTTGCATTAGCCTCAAAC	1190
1191	GTCTGATGACTAACAGGGTGGTGGTGGCACACCATGAGGTAAGCTCAGCCCCCTGCCCTCCATCTCCCACC	1260
1261	CTAACCATCATCACCCCTCTCTCTTTCCCTGACAGTGCTGAGGGCGGCATTAAAGAGGAAGTCCTGGCTGCAG	1330
	alLeuArgArgHis***	
1331	ACACCTGCTTCTGATTCACAAAGGGGCTTTTTCCTCAACCCTGTGGCCCTCATCTTTTCCTTTGGAATTAG	1400
1401	TGATAAAGGAATCAGAAAATGGAGAGACTGGGTGCCCTGACCCCTGTACCCCAAGGCAGTCGGTTCACCTGG	1470
1471	GTGCCATGAAGGGCCTGGTGAGCCAGGGGTTGGGTCCCTGAGGCTTTTA	1519

FIG.7B

[illegible]

20
eu
ier
la
40

le
la
ber

09asp
la
ier

80 Ala. Chr. ---

100
Per

r1

120 Leu --- Ser

130 131
Arg Tyr
Lys --- His

130 131
Arg Tyr
Lys --- His